

# Lung deposition of budesonide from the novel dry powder inhaler Airmax<sup>TM</sup>

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**Abstract** The deposition of budesonide at fast (60 l min<sup>-1</sup>) and slow (30 l min<sup>-1</sup>) inspiratory flow rates from Airmax<sup>TM</sup>, a new multi-dose dry powder inhaler, was compared with that from Turbuhaler<sup>®</sup> and a standard pressurized metered dose inhaler (pMDI). Twelve patients with mild to moderate asthma took part in a five-way randomized cross-over study, and inhaled a single nominal dose of 200 µg budesonide, labelled with <sup>99m</sup>Tc, on each study day. Deposition was determined by gamma scintigraphy.

At the fast flow rate, Airmax<sup>TM</sup> and Turbuhaler<sup>®</sup> deposited  $25.8 \pm 6.5\%$  (mean  $\pm$  SD) and  $29.8 \pm 6.9\%$ , respectively, of the delivered dose in the whole lung ( $P = 0.080$ ). At the slow flow rate, Airmax<sup>TM</sup> deposited  $28.3 \pm 5.6\%$ , Turbuhaler<sup>®</sup>  $22.7 \pm 5.6\%$  and pMDI  $12.1 \pm 3.4\%$ . Using data on emitted doses determined *in vitro*, it was estimated that Airmax<sup>TM</sup> deposited  $53.1 \pm 13.3$  µg and  $43.6 \pm 8.6$  µg budesonide in the lungs at 60 l min<sup>-1</sup> and 30 l min<sup>-1</sup> respectively, whilst Turbuhaler<sup>®</sup> deposited  $48.3 \pm 11.2$  µg at 60 l min<sup>-1</sup> and  $24.2 \pm 6.0$  µg at 30 l min<sup>-1</sup>.

In conclusion, lung deposition of budesonide from Airmax<sup>TM</sup> was comparable to that of Turbuhaler<sup>®</sup> at a high flow rate but was markedly superior to Turbuhaler<sup>®</sup> and pMDI at a lower flow rate. Unlike Turbuhaler<sup>®</sup>, Airmax<sup>TM</sup> performs with relative flow-rate independence. © 2002 Elsevier Science Ltd.

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**Keywords** Turbuhaler<sup>®</sup>; gamma scintigraphy; asthma; clinical study; MDI; planar imaging.

## INTRODUCTION

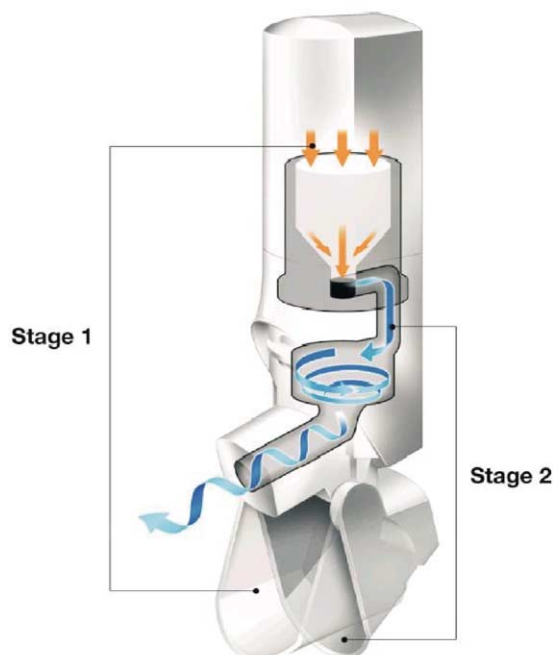
Inefficient inhaler use has long been recognized as a major problem for many patients using pressurized metered dose inhalers (pMDIs) who have difficulty in co-ordinating actuation of the device with inhalation (I). Such problems, together with the phasing out of the chlorofluorocarbon propellants used in the original formulations of MDIs, have resulted in the development of dry powder inhalers (DPIs). Patients generally find DPIs easier to use than pMDIs since they are breath-actuated and do not require co-ordination of actuation and inhalation. Furthermore DPIs operate without the need for potentially environmentally damaging propellants. However *in vivo* lung deposition can be influenced by the patient's inspiratory flow rate, and this may be particularly relevant for patients with severe asthma, the elderly and young children (2). Pulmicort Turbuhaler<sup>®</sup> (AstraZeneca, Lund, Sweden) is a multi-dose DPI that has been widely used for the delivery of budesonide powder. How-

ever, it is well documented that the amount of drug delivered from the Turbuhaler<sup>®</sup> varies greatly from dose to dose, and that particularly the fine particle dose is reduced significantly when used with a low inspiratory flow rate (3,4).

Airmax<sup>TM</sup> is a trademark of Yamanouchi Europe BV (Leiderdorp, The Netherlands) for a novel multi-dose (200 doses) DPI, which utilizes proprietary technology known as the X-ACT<sup>TM</sup> system (Fig. 1). This active-metering, cyclone-separator technology was designed to provide accurate and consistent dosing to the patient largely independent of inspiratory effort. Unlike other devices which rely on gravity, X-ACT<sup>TM</sup> uses controlled air pressure from an internal pump to exactly meter the dose. The inhaler is simply operated by opening the mouthpiece cap, inhaling and closing again. Closing of the cap triggers the precise dose counter. When the patient inhales, the dose is transported into the cyclone separator, which separates the drug from its lactose carrier and produces a high fine particle dose. Gravimetric studies and studies with multi-stage liquid impingers have shown typical relative standard deviations of dose consistency of 5%, emitted doses between 90–105% of label claim and fine particle fractions between 49–59% (5,6).

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**Fig. 1.** Diagram of Airmax<sup>TM</sup> inhaler with stage 1 (active metering) and 2 (cyclone separator).

The aim of the present study was to confirm the *in vitro* results using a validated gamma scintigraphic technique (7–9), and to compare the delivery of budesonide from Airmax<sup>TM</sup> with that from Turbuhaler<sup>®</sup> at different flow rates and with that from a pMDI. In order to make the data as clinically relevant as possible, results were expressed both as percentage of delivered dose and as mass of budesonide deposited in the lungs.

## METHODS

### STUDY POPULATION

Sixteen volunteers aged 18–55 years with a diagnosis of asthma at least 6 months prior to study entry were screened, of whom 13 were subsequently entered into the study. All patients had within the previous 2 years demonstrated a forced expiratory volume in 1 sec (FEV<sub>1</sub>) at least 60% predicted for their height and gender, and a reversibility of at least 10% in FEV<sub>1</sub> following inhalation of a standard 200 µg dose of salbutamol from a pMDI. Patients were excluded if they had upper or lower respiratory tract infection within the previous 2 weeks. All patients gave written informed consent to their participation after full explanation of the nature of the study, which was approved by the Quorn Research Review Committee, Leicestershire, UK, and performed in accordance with the Declaration of Helsinki.

### STUDY DESIGN

The study was carried out according to a randomized, open label, cross-over design during five study periods, each separated by a minimum period of 44 h. During each study period patients inhaled  $2 \times 100$  µg of salbutamol followed 15–30 min later by a single (200 µg) dose of budesonide labelled with up to 10 MBq <sup>99m</sup>Tc administered either from Airmax<sup>TM</sup> or Turbuhaler<sup>®</sup> at targeted peak inspiratory flow rates (PIFR) of 30 l min<sup>-1</sup> or 60 l min<sup>-1</sup>, and from a standard pMDI (Pulmicort<sup>®</sup>) at a targeted PIFR of 30 l min<sup>-1</sup>. Subjects were instructed to inhale deeply and to follow inhalation with a 10 sec breath-hold and exhalation via a low resistance filter. Each subject practiced the inhalation manoeuvre with a placebo device until the inhalation technique had been mastered. A Vitalograph MDI–Compact Spirometer (Vitalograph Ltd, Maids Moreton, Buckinghamshire, U.K.) connected in series with the inhaler devices recorded peak inspiratory flow rates, inhaled volumes and breath holding pauses. A Microloop spirometer (Micro Medical, Rochester, U.K.) was used to record FEV<sub>1</sub> before dosing and then 60 min post-dosing.

### RADIOLABELLING OF BUDESONIDE

Budesonide from the Turbuhaler<sup>®</sup> was radiolabelled as described previously (10). Briefly, the radiolabel (<sup>99m</sup>Tc) was extracted from saline into methyl ethylketone, and after removal of the solvent by evaporation, was redissolved in water and mixed with budesonide powder. The water was then removed by freeze-drying and the radiolabelled powder transferred to an empty Turbuhaler. For Airmax<sup>TM</sup>, a similar method was used to obtain radiolabelled budesonide powder, 100 mg of which was blended with lactose (2050 mg) in a Turbula mixer (42 rpm) for 30 min. Each Airmax<sup>TM</sup> device was filled with 730 mg of this blend.

The method for the pMDI was as follows: the radiolabel (<sup>99m</sup>Tc) was extracted into methyl ethylketone and transferred to an empty pMDI canister. After removal of the solvent the contents of a full canister previously cooled in liquid nitrogen were added to the residue and a new metering valve was crimped in place. The canister was sonicated for 10 min in order to ensure even dispersion of the radiolabel throughout the formulation.

In order to show that the radiolabel was a valid marker for budesonide, the size distributions of drug before labelling, of drug after labelling and of <sup>99m</sup>Tc radiolabel were compared. A High Precision Multistage Liquid Impinger (HPMLI, Copley Instruments, Nottingham, U.K.) was used for the two DPIs, and an Andersen Cascade Impactor (ACI, Copley Instruments) for the pMDI. The test method was based on pharmacopeial standards i.e. testing at a pressure drop of 4 kPa across the device for the DPIs and a flow rate of 28.3 l min<sup>-1</sup> for the pMDI. The

objective was to show that the size distributions of the products were not changed significantly by the radiolabelling procedure, and that the radiolabel and drug matched one another across the full range of particle size bands.

## GAMMA SCINTIGRAPHY

Immediately following administration of the radiolabelled formulation, posterior and anterior views of the chest and a right lateral view of the oropharynx were recorded using a gamma camera (General Electric Maxicamera, Milwaukee, WI, U.S.A.) connected to a Park Medical computer system (Farnborough, U.K.). On one study day, unless available from a previous study within the previous 2 years, a posterior lung ventilation scan was performed on each patient using the radioactive inert gas  $^{81\text{m}}\text{Kr}$  in order to define the edges of the lung fields. The lungs were subdivided into central, intermediate and peripheral regions of interest as previously described (11), thus enabling the percentage of the dose in each lung zone to be determined and the peripheral lung zone/central lung zone deposition ratio to be calculated. The counts obtained within these regions were corrected for background radioactivity, radioactive decay, acquisition time and for tissue attenuation of gamma rays (12). In regions where both anterior and posterior images were recorded, the geometric mean of counts in both images was calculated prior to correction for tissue attenuation. Deposition in the oropharynx included activity adhering to the mouth and oropharynx together with any swallowed activity detected in the oesophagus, stomach and intestine and activities deposited on the mouthpiece of the exhalation filter. Since the mouthpiece of the Airmax™ cannot be separated from the body of the device, it was not possible to quantify deposition on the Airmax™ mouthpiece. Data for all three devices were expressed as percentage of delivered (emitted) dose from the sum of corrected total body counts and those on the exhaled air filter.

The actual masses of budesonide deposited in the lungs were calculated by using actual delivered masses at the relevant flow rates determined by *in vitro* analysis. Using an HPMLI delivered doses at the flow rates of  $60\text{ l min}^{-1}$  and  $30\text{ l min}^{-1}$  for each DPI ( $n=3$ ) were first determined. Mean dose delivered by the pMDI was assumed to be equal to the nominal dose of  $200\text{ }\mu\text{g}$ . Lung deposition values expressed as mass of budesonide were calculated as (% delivered dose in lungs)  $\times$  (mean measured delivered dose) / 100.

## STATISTICAL ANALYSIS

The study was designed to detect differences between the patterns of lung deposition from different devices at

the two flow rates. Since clinically relevant differences were unknown, an arbitrary 4% difference in total lung deposition was selected for power calculations. Based on previous studies which had demonstrated whole lung deposition of a range of inhalers averaging 15% of the dose, with a standard deviation of 3% of the dose, it was calculated that 10 evaluable patients would be needed to detect a difference of 4% with  $\alpha=0.05$  and a power of 80%.

Three contrasts were defined and were statistically analysed using analysis of variance (ANOVA) model, including terms for patient, treatment and sequence. These contrasts were: Airmax™ at  $60\text{ l min}^{-1}$  vs. Turbuhaler® at  $60\text{ l min}^{-1}$ , Airmax™ at  $60\text{ l min}^{-1}$  vs.  $30\text{ l min}^{-1}$  and Turbuhaler® at  $60\text{ l min}^{-1}$  vs.  $30\text{ l min}^{-1}$ . Because the least square means % deposition and mass deposited calculated from ANOVA did not differ from the actual crude means, only the crude means and their standard deviation are reported here. All reported *P*-values are based on this ANOVA, and a *P*-value of  $<0.05$  was considered statistically significant.

## RESULTS

### RADIOLABELLING VALIDATION

The results of the radiolabelling validation experiments are shown in Table 1. For all devices there was a good match between the fine particle fractions (FPFs) of delivered dose for the drug before labelling, the drug after labelling and the radiolabel itself. Hence the radiolabel was considered to be a valid marker for the drug for all three products. The radiolabel FPFs of the inhalers used on study days were determined before dosing, and were shown to be within the range of values determined in the prestudy validation testing.

### PATIENTS

Demographic variables of the patients are shown in Table 2. Of the 13 patients that entered the study, 12 completed the  $60\text{ l min}^{-1}$  arms with the DPIs and 11 completed the  $30\text{ l min}^{-1}$  arms.

### Inhalation manoeuvres and lung function

Table 3 displays details of the inhalation manoeuvres for each device and of lung function pre- and post-dosing. Mean PIFR was above target for Airmax™ and pMDI, and close to target for Turbuhaler®. Mean breath-holding times and inhaled volumes were comparable for all five treatment regimens.

**TABLE 1.** Mean (sd) Results of the radiolabelling validation assessment

	Flow rate	Fine particle fractions (% delivered dose)		
	$\text{l min}^{-1}$	Drug before labelling (%)	Drug after labelling	Radiolabel (%)
Airmax <sup>TM</sup> (n = 5)	70	$42.7 \pm 1.9$	$40.6 \pm 4.2$	$43.4 \pm 3.2$
Turbuhaler <sup>®</sup> (n = 5)	60	$57.6 \pm 1.3$	$57.7 \pm 3.4$	$56.0 \pm 6.3$
pMDI (n = 5)	28.3	$35.9 \pm 3.1$	$34.6 \pm 1.8$	$40.1 \pm 6.1$

**TABLE 2.** Mean demographic and baseline characteristics of randomized patients

Gender	Male	6
	Female	7
Age (years)	Mean (range)	34.7 (20–52)
Height (cm)	Mean (range)	172.3 (154–186)
Weight (kg)	Mean (range)	73.4 (59–105)
Race	Caucasian	12 (92.3%)
	Asian	1 (7.7%)
Baseline FEV <sub>1</sub> (l)	Mean (range)	3.05 (2.20–3.94)
% Predicted FEV <sub>1</sub> at baseline	Mean (range)	86.7 (67.1–104.5)

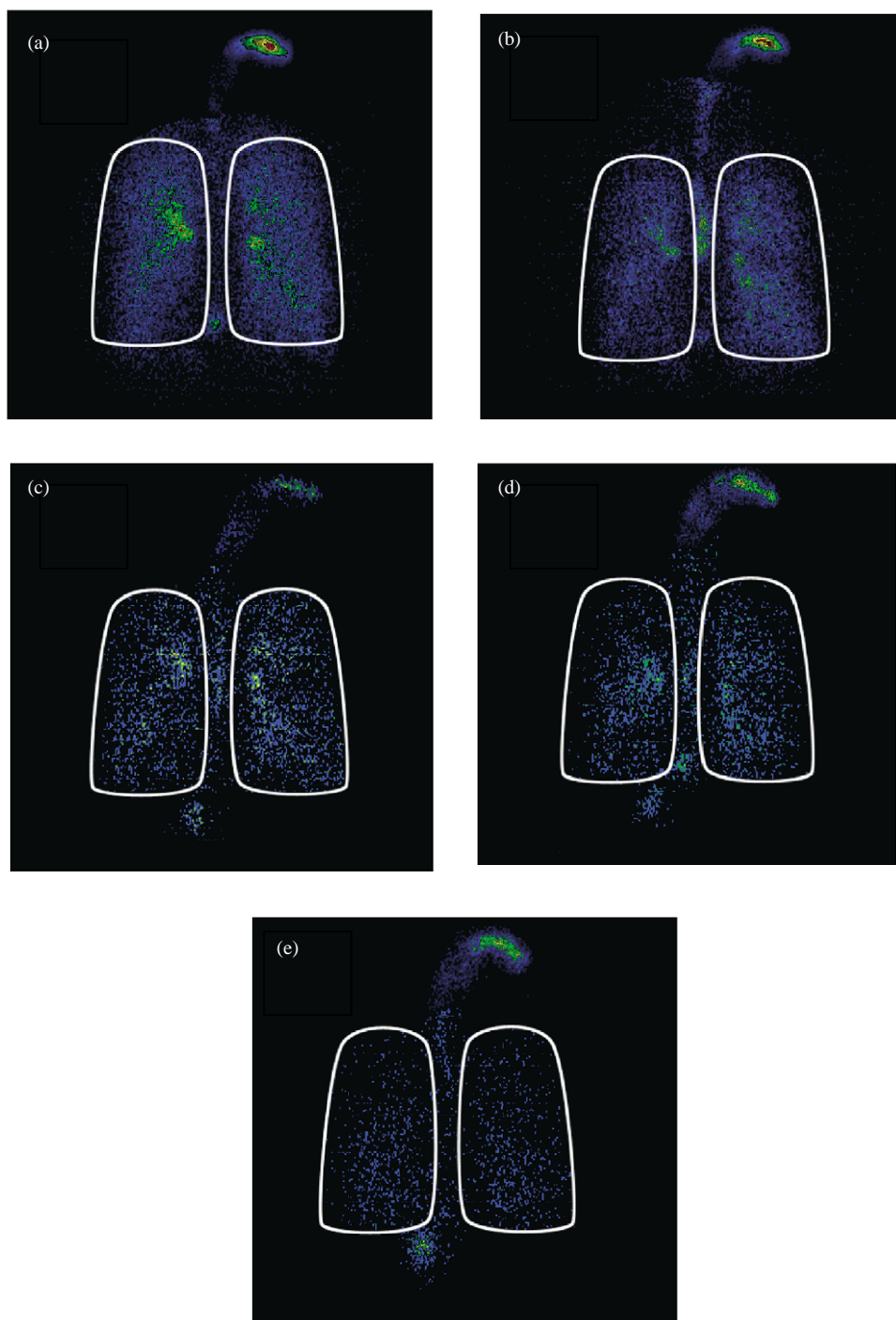
**TABLE 3.** Mean average and peak inspiratory flow rates, breath-holding times, inhaled volumes and FEV<sub>1</sub> pre- and 60 min post-dosing

	Airmax <sup>TM</sup>		Turbuhaler <sup>®</sup>		pmdi
Targeted PIFR $\text{l min}^{-1}$	60	30	60	30	30
n	12	11	12	11	11
Peak inspiratory flow ( $\text{l min}^{-1}$ )	71.64	37.45	59.75	31.60	38.91
(sd)	(11.81)	(6.33)	(13.80)	(3.24)	(13.76)
Inhaled volume (l)	2.49	2.73	2.99	3.04	2.60
(sd)	(0.89)	(0.77)	(0.99)	(1.03)	(1.0)
Breath-holding time (sec)	10.0	10.4	10.0	9.5	10.6
(sd)	(1.0)	(1.8)	(1.5)	(0.9)	(1.2)
Pre-dose FEV <sub>1</sub> (l)	3.00	2.89	2.98	2.80	2.98
(sd)	(0.57)	(0.59)	(0.51)	(0.41)	(0.52)
60 min post-dose FEV <sub>1</sub> (l)	3.24	3.18	3.25	3.25	3.28
(sd)	(0.52)	(0.52)	(0.52)	(0.52)	(0.56)

## DEPOSITION DATA

Scintigraphic images showing deposition patterns for each of the five dosing regimens are shown in Fig. 2. The mean ( $\pm$  sd) whole lung deposition expressed as percentage of delivered dose was  $25.8 \pm 6.5\%$  and  $29.8 \pm 6.9\%$  for Airmax<sup>TM</sup> and Turbuhaler<sup>®</sup>, respectively, at the fast inspiratory flow rate ( $60 \text{ l min}^{-1}$ ). This difference was not statistically significant ( $P = 0.080$ ). At  $30 \text{ l min}^{-1}$ , Airmax<sup>TM</sup> deposited  $28.3 \pm 5.6\%$  and Turbuhaler<sup>®</sup>

$22.7 \pm 5.6\%$  of the delivered dose in the whole lung. The small increase in deposition for Airmax<sup>TM</sup> at the lower flow rate was not statistically significant ( $P = 0.208$ ), whereas the decrease in performance at lower flow rate for Turbuhaler<sup>®</sup> was significant ( $P = 0.003$ ). Whole lung deposition was lowest for the pMDI ( $12.1 \pm 3.4\%$ ), while oropharyngeal deposition was highest ( $86.8 \pm 3.8\%$ ) with the pMDI. Regional deposition patterns were similar for all treatments with the peripheral zone being the



**FIG. 2.** Scintigraphic images obtained using Airmax™ at (a)  $60 \text{ l min}^{-1}$  (b)  $30 \text{ l min}^{-1}$ ; Turbuhaler® at (c)  $60 \text{ l min}^{-1}$  (d)  $30 \text{ l min}^{-1}$  and (e) a pMDI at  $30 \text{ l min}^{-1}$ .

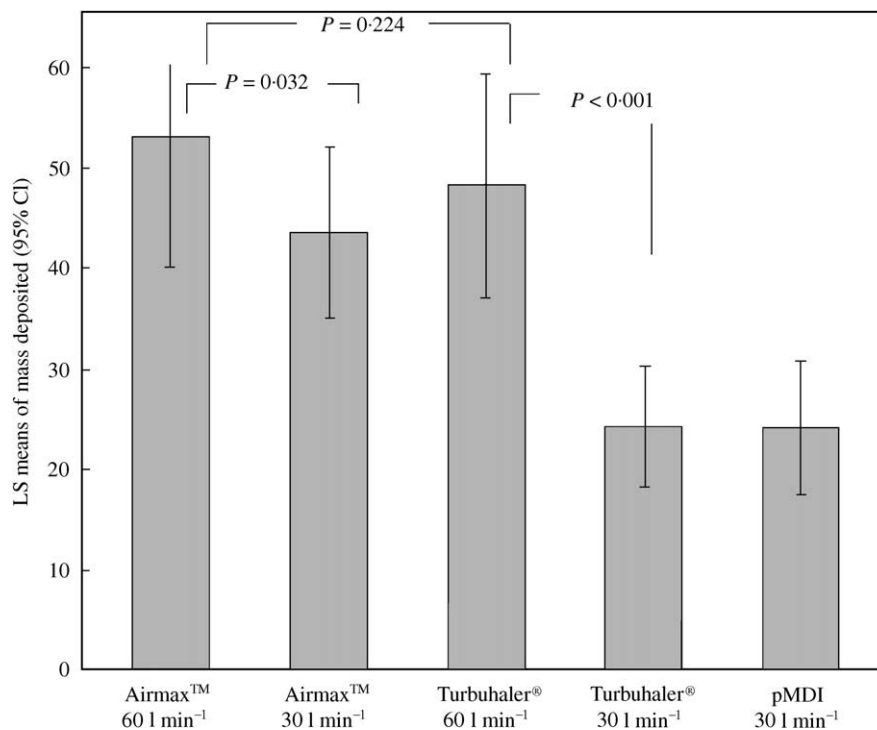
major deposition site (Table 4). The peripheral lung zone/central lung zone deposition ratios tended to be higher for Airmax™ than for Turbuhaler® but these differences were small.

Using HPMLI testing at  $60 \text{ l min}^{-1}$ , we found that Airmax™ delivered  $206 \pm 4 \mu\text{g}$  budesonide and

Turbuhaler®  $162 \pm 33 \mu\text{g}$  budesonide (nominal doses  $200 \mu\text{g}$  for both products). At a flow rate of  $30 \text{ l min}^{-1}$  delivered dose dropped to  $154 \pm 27 \mu\text{g}$  for Airmax™ and to  $107 \pm 39 \mu\text{g}$  for Turbuhaler®. Using the mean delivered dose values we estimated that in patients inhaling at a target flow of  $60 \text{ l min}^{-1}$  Airmax™ deposited

**TABLE 4.** Summary of deposition data based on delivered dose of budesonide by inhaler and inspiratory flow

	Airmax <sup>TM</sup>		Turbuhaler <sup>®</sup>		pMDI
Targeted PIFR l min <sup>-1</sup>	60	30	60	30	30
n	12	11	12	11	11
Whole lung (%)	25.8	28.3	29.8	22.7	12.1
(SD)	(6.5)	(5.6)	(6.9)	(5.6)	(3.4)
Central lung (%)	6.5	7.4	8.5	6.5	3.0
(SD)	(1.7)	(2.1)	(2.1)	(2.5)	(0.7)
Intermediate lung (%)	8.6	9.6	10.1	7.9	3.9
(SD)	(2.0)	(2.4)	(2.5)	(2.3)	(0.9)
Peripheral lung (%)	10.7	11.4	11.2	8.3	5.2
(SD)	(3.3)	(2.0)	(3.0)	(4.1)	(2.0)
Oropharynx (%)	73.6	71.4	69.1	76.0	86.8
(SD)	(6.7)	(5.5)	(7.0)	(6.2)	(3.8)
Exhalation filter (%)	0.3	0.6	1.3	1.1	1.1
(SD)	(0.2)	(0.4)	(3.0)	(0.8)	(0.7)
Peripheral/central ratio	1.7	1.7	1.4	1.5	1.8
(SD)	(0.4)	(0.5)	(0.3)	(0.8)	(0.6)

**FIG. 3.** Mass of budesonide (in  $\mu\text{g}$ ) deposited by inhaler and inspiratory flow.

53.1  $\pm$  13.3  $\mu\text{g}$  and Turbuhaler 48.3  $\pm$  11.2  $\mu\text{g}$  in the lungs (Fig. 3). As with percentage deposition data, the estimated mass of budesonide deposited in the whole lungs with Airmax<sup>TM</sup> did not differ significantly from the mass deposited by Turbuhaler<sup>®</sup> at 60 l min<sup>-1</sup> ( $P=0.224$ ). The estimated mass deposited in the lungs

dropped to 43.6  $\pm$  8.6  $\mu\text{g}$  for Airmax<sup>TM</sup> at 30 l min<sup>-1</sup> ( $P=0.032$  compared to 60 l min<sup>-1</sup>). Turbuhaler<sup>®</sup> deposited in the lungs at 30 l min<sup>-1</sup> only about half of the amount compared to 60 l min<sup>-1</sup> (24.2  $\pm$  6.0  $\mu\text{g}$ ,  $P<0.001$ ) and this amount was similar to that deposited by pMDI (24.1  $\pm$  6.7  $\mu\text{g}$ ).

## Safety

A total of 11 mild to moderate adverse events were reported by nine patients, of whom five reported adverse events before the first treatment period. Adverse events included headache, rhinitis and conjunctivitis. None of these were considered to be related to the study medication or procedures. There were no serious adverse events. There was no evidence of bronchoconstriction for any of the study regimens.

## DISCUSSION

The present study showed that the novel multi-dose dry powder inhaler, Airmax™, deposited a mean 26% of the delivered dose (mean 53 µg budesonide) in the lungs at the fast flow rate of 60 l min<sup>-1</sup>. This amount is similar to that delivered by Turbuhaler® at this flow rate. At low inhaled flow rate (30 l min<sup>-1</sup>) the performance of Airmax™ remained virtually unchanged, whereas Turbuhaler® delivered significantly less budesonide. Both dry powder inhalers were superior to pMDI when used at high inspiratory flow rates. The regional lung distribution patterns were broadly similar between the different inhalers and flow rates investigated.

The data obtained in the present study are consistent with those obtained in previous studies with Turbuhaler® and pMDIs. At a peak inspiratory flow rate (PIFR) of 60 l min<sup>-1</sup>, lung deposition from the Turbuhaler® averages between 14% and 32% of the metered dose (13–17). A halving of PIFR to 30 l min<sup>-1</sup> has been shown previously to approximately halve lung deposition (16), while lung deposition from a budesonide pMDI has been shown to be approximately half of that from a Turbuhaler® (13,14), when both Turbuhaler® and pMDI were used optimally.

In the present study there was a close match between actual PIFR and target values for Turbuhaler®, but with Airmax™ and with the pMDI the PIFR tended to be higher than target. This could have biased the results towards a better performance for Airmax™. However, the difference between Turbuhaler® (PIFR 59.8 l min<sup>-1</sup>) and Airmax™ (71.6 l min<sup>-1</sup>) closely resembled the difference (i.e. about 70 l min<sup>-1</sup> vs. 60 l min<sup>-1</sup> for Airmax™ and Turbuhaler®, respectively) observed in *in vitro* studies (Table I) when both inhalers are tested at a pressure drop of 4 kPa as required by Pharmacopoeial guidelines (18). This difference is caused by the higher internal resistance of the Turbuhaler®. This suggests that the inspiratory effort applied by the patients in this trial was similar for both Airmax™ and Turbuhaler® and hence the comparison is justified.

The use of gamma scintigraphy, as other imaging techniques, does not allow direct quantification of the mass of drug deposited. In order to understand as fully as pos-

sible the clinical relevance of our findings, we estimated lung deposition expressed not only as percentage of delivered dose, but also as mass of budesonide deposited into the lungs, based on separate laboratory measurements of delivered (emitted) dose. In our *in vitro* analysis we showed that Airmax™ delivered 103% of the label claim at 60 l min<sup>-1</sup> and 77% at 30 l min<sup>-1</sup>, hence there was a drop in estimated mean mass deposited in the lungs of about 10 µg when the flow rate through the Airmax was halved. For Turbuhaler® this drop in performance was accentuated as the *in vitro* method showed that at 60 l min<sup>-1</sup> typically only 80% of the label claim was emitted and at 30 l min<sup>-1</sup> this dropped to 54% of the label claim. These data were consistent with those reported by other investigators (15,16). As a consequence partly of reduced percentage deposition, and partly of reduced delivered dose, the mass of budesonide deposited in the lungs was halved when the inhaled flow rate through the Turbuhaler® was reduced from 60 l min<sup>-1</sup> to 30 l min<sup>-1</sup>. Lung deposition of budesonide from Turbuhaler® at 30 l min<sup>-1</sup> was similar at around 24 µg to lung deposition achieved by the pMDI at this flow rate.

There have been few studies to quantify the mass of drug deposited into the lungs through imaging techniques, and expressing the results in this way may give a better correlation with clinical findings. Hence the results of lung deposition studies may be considered as a 'bridge' between the *in vitro* testing programme and clinical trials carried out to assess the efficacy of a novel product in man (19). The clinical response to inhaled anti-asthma drugs may depend not only upon the total amount of drug deposited in the lungs, but also upon the regional deposition pattern within the airways (20). This was expressed in the present study as the peripheral/central (P/C) ratio which has been shown to correlate with the relative amounts of drug deposited in the tracheobronchial and alveolated airways of the lungs (21). The similar P/C ratios for Airmax™ and Turbuhaler® in this study suggest that both devices fractionate the dose between the two major anatomical regions of the lungs in a broadly similar manner. The P/C ratios in this study were more typical of those often seen in healthy subjects, despite this being a patient study. This could be a result of the predose administration of salbutamol, which was done in order to minimise day-to-day variation in lung function in this cross-over study.

We conclude that lung deposition of budesonide from Airmax™ and Turbuhaler® are similar when used by patients at 'fast' inspiratory flows of 60 l min<sup>-1</sup>. However, lung deposition from Airmax™ at low flow rates is markedly superior to both Turbuhaler® and pMDI. Unlike Turbuhaler®, Airmax™ DPI performs relatively independently of flow rate and hence inspiratory effort.

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